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09/601,582	12/04/2000	Qingyun Liu	20052YP	8319

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EXAMINER
KAUFMAN, CLAIRE M

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1646	5

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/601,582	Applicant(s) LIU ET AL.	
	Examiner Claire M. Kaufman	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *6,10-13,15 and 17* is/are withdrawn from consideration.

5)☒ Claim(s) *1,2,4,5 and 7* is/are allowed.

6)☒ Claim(s) *3,8,9,14,16,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-19* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Notice to Comply* .

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-5, 7-9, 14, 16, 18 and 19, drawn to HG20 DNA, vector, host cell, protein, heterodimer comprising the protein, method of detecting binding of GABAB receptors, method of producing functional GABAB receptors, and method of expressing an amino-terminal truncated HG20.

Group II, claim(s) 10-11, drawn to a polypeptide consisting of a coiled-coil domain.

Group III, claim(s) 12-13, drawn to DNA encoding a GABABR1a polypeptide and GABABR1a protein.

Group IV, claim(s) 15, drawn to method of identifying agonists and antagonists of HG20..

Group V, claim(s) 17, drawn to antibody that binds HG20.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Pursuant to 37 C.F.R. 1.475(d), this Authority considers that the main invention in the instant application comprises the first-recited product, DNA encoding HG20, and the first-recited method of using that product, namely the method of detecting binding to GABAB receptors. Note that there is no method of making the polynucleotide. Also included in the first group is the encoded protein and the process of producing the encoded protein, in addition to a heterodimer, vector and host cell. Further, pursuant to 37 C.F.R. 1.475(b)-(d), the materially and functionally dissimilar product of groups II and V and the additional methods of groups III-IV do not correspond to the main invention. This Authority therefore considers that the

several inventions do not share a special technical feature within the meaning of PCT Rule 13.2 and thus do not relate to a single general inventive concept within the meaning of PCT Rule 13.1.

During a telephone conversation with Joseph A. Coppola on February 12, 2002, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-5, 7-9, 14, 16, 18 and 19. Affirmation of this election must be made by applicant in replying to this Office action. Claims 6, 10-13, 15 and 17 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Note that claim 6 could not be assigned to a group since it is an incomplete and unexaminable claim.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Sequences

This application contains sequence disclosures that are encompassed by the definitions for nucleic and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth in the attached Notice to Comply with Requirements for Patent Applications Containing Nucleic Sequence and/or Amino Acid Sequence Disclosures. In the current application, a CRF and Sequence Listing is required, but not none was submitted. The CRF from the priority PCT is not transferable.

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The first sentence of the specification should reference that : This application is the National Stage of International Application No. PCT/US99/02361, filed February 3, 1999, and published in English, which claims benefit of U.S. Provisional....

Also, the provisional application number should have a "/" after "60" (60/073,767).

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). The address of inventor Kolakowski was changed but not initialed.

Claim Objections

Claim 14 is objected to because of the following informality: in line 4 of the claim "c1'omprising" should be "comprising". Appropriate correction is required.

Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Since claim 3 is drawn to a DNA that hybridizes to a reference DNA and claim 2 is drawn to the reference DNA, the dependent claim could be infringed by something that does not infringe the base claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 16, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite because it is not clear what conditions are intended by "stringent"

hybridization conditions, since the description gives examples of high stringency (pages 15-16), but it is unclear if moderate and low stringency conditions are also intended to be included.

Claim 16 is indefinite because it is unclear if the polypeptides of the heterodimers are those expressed from the vectors or are endogenous (see claim 14(b) for example of clear expression language, *i.e.*, a statement that the receptor subunit within the vector is expressed).

Claim 18 is indefinite because it is unclear what the truncation is--that is, if it the first amino-terminal amino acid or it can be a larger fragment, and if it can be a fragment--how big a fragment (*e.g.*, truncation of 95% of the HG20 protein). It is not clear from the specification (p. 18, lines 4-6) if the truncation is meant to be limited to up to the first 51 amino acids of SEQ ID NO:2.

Claim 19 is indefinite because in the last line, it is not clear if the reference to "a non-HG20 amino acid sequence" means anything that is not one of the sequences listed earlier in the claim (*e.g.*, a non-HG20 amino acid sequence could be amino acids 61-941 of SEQ ID NO:2) but can still be highly related to SEQ ID NO:2. This rejection could be obviated, if appropriate, by substitution of the phrase cited with –a heterologous amino acid sequence--, *i.e.*, a sequence from another protein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (claim 3) a DNA that hybridizes to the DNA of SEQ ID NO:1 under conditions of high stringency as shown in the example on page 14 in lines 7-14 and which can form a functional GABAB receptor as defined on page 11 in lines 7-8 and (claim 18) a method of expression a truncated version of HG20 protein of SEQ ID NO:2 which truncate can form a functional GABAB receptor as defined on page 11 in lines 7-8, does not reasonably provide enablement for a DNA or truncate without the above structural or functional properties.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The specification teaches the HG20 protein has the full-length sequence of SEQ ID NO:2 and of that a signal sequence from amino acid 1-51 of SEQ ID NO:2. This full-length or mature form can form a functional GABAB receptor when hetereodimerized with GABABR1a or GABABR1b to have a functional response (see page 11, lines 9-13 of the specification). What the specification has not taught is how to use a DNA that does not encode a HG20 which is "functional" or how to use an HG20 protein truncate which is not "functional". Nor has the specification taught a DNA sequence other than SEQ ID NO:1 or fragment thereof which encodes a functional HG20 protein, though the skilled artisan would readily recognize that a degenerate DNA sequence encoding SEQ ID NO:2 would produce a functional HG20 protein.

There were only 2 other GABAB receptor proteins know at the time of filing of the instant application (Kaupmann et al., 1997, Nature 386:239-246). The field of GABAB receptors was new in molecular biology terms, so the skill in the art was not high. While these 3 receptors share some common structures and conserved amino acids (see for example Figs. 24A-B of the specification), there is little information in the prior art or specification to enable the skilled artisan to predict which amino acids are critical, which can be substituted and with what. As a result, given a DNA sequence encoding a protein that was not identical in structure to SEQ ID NO:2 or the mature form thereof, one would not know how to use it if it did not have a disclosed function. Also, if the DNA sequence did not share high identity with SEQ ID NO:1 or did not encode a protein highly identical to SEQ ID NO:2, one skilled in the art would not be able to predict if it encoded a protein that functioned the same as the HG20 protein of SEQ ID NO:2. If it did not function the same by forming a functional GABAB receptor when heterodimerized to GABABR1a or –b, neither the specification or prior art provides guidance of

how to use it. As a result, it would require undue experimentation to practice the claimed invention commensurate in scope with the claim.

Claims 14, 16 and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite HG20 without any structural limitation. The specification discloses SEQ ID NO:1, the sequence of the nucleic acid encoding the HG20 protein having the sequence of SEQ ID NO:2. SEQ ID NO:1 meets the written description and enablement provision of 35 USC 112, first paragraph. However, the claims are directed to or encompass sequences unrelated to SEQ ID NO:2, corresponding sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity, and so forth. None of these sequences meets the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptide, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to

lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NO:2 or at least amino acids 57-941 of SEQ ID NO:2 (the mature form), but not the full breadth of the claim meets the written description provision of 35 U.S.C. § 112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by GenBank Database Accession Numbers H14151, Z43654 or T07621.

GenBank Database Accession Numbers H14151, Z43654 and T07621 each teach isolated DNA molecules that would hybridize under stringent conditions to the DNA described of claim 2 because there is about 95% identity over at least 341 consecutive nucleotides between the DNA of claim 2 and each of the GenBank DNAs (see for example the attached sequence comparison for Accession Z43654, nucleotides 2490-2707 of SEQ ID NO:1).

35 U.S.C. § 119(e) states that:

> (e)
> (1) An application for patent filed under section 111(a) or section 363 of this title for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in a provisional application filed under section 111(b) of this title, by an inventor or inventors named in the provisional application, shall have the same effect, as to such invention, as though filed on the date of the provisional application filed under section 111(b) of this title, if the application for patent filed under section 111(a) or section 363 of this title is filed not later than 12 months after the date on which the provisional application was filed and if it contains or is amended to contain a specific reference to the provisional application. No application shall be entitled to the benefit of an earlier filed provisional application under this subsection unless an amendment containing the specific reference to the earlier filed provisional application is submitted at such time during the pendency of the application as

> required by the Director. The Director may consider the failure to submit such an amendment within that time period as a waiver of any benefit under this subsection. The Director may establish procedures, including the payment of a surcharge, to accept an unintentionally delayed submission of an amendment under this subsection during the pendency of the application....

Applicant is advised that the instant application can only receive benefit under 35 USC § 119(e) from a provisional application which meets the requirements of 35 USC § 112, first paragraph, with respect to the now claimed invention. Because the instant application does not meet the requirements of 35 USC § 112, first paragraph, for those reasons given above because of the absence of a sufficient disclosure of a heterodimer comprising HG20 and GABABR1a or –R1b, the provisional application also does not meet those requirements and, therfoere, is unavailable for benefit of priority under 35 UCS § 119(e). Therefore for claims drawn to a heterodimer or methods of using or producing a heterodimer, the priority date is the filing date of PCT/US99/02361, filed February 3, 1999.

Claims 8, 9, 14 and 16 rejected under 35 U.S.C. 102(a) as being anticipated by White et al. (Nature 396: 679-682, Dec. 1998).

White et al. teach human GABABR2, which has the same sequence as HG20 of SEQ ID NO:2 of the instant application, as well as production of a functional heterodimeric GABAB receptor by expression of vectors comprising GABABR2 and either GABABR1a or -R1b in HEK293T cells (p. 681, col. 2, second full paragraph). Ligand binding was quantified for the expressed GABAB receptor. Also shown is that the heterodimer is held together by the coiled-coil domains (p. 680, sentence bridging cols. 1-2).

Claims 14 and 16 rejected under 35 U.S.C. 102(a) as being anticipated by Jones et al. (Nature 396: 674-678, Dec. 1998) or Kaupmann et al. (Nature 396: 683-687, Dec. 1998) or Kuner et al. (Science 283: 74-77, Jan. 1999).

Jones, Kaupman, and Kuner et al. teach rat GABABR2 (Fig. 1a), which is 97% identical to HG20 of SEQ ID NO:2 of the instant application. Also taught is production of a functional heterodimeric GABAB receptor by expression of vectors comprising GABABR2 and either GABABR1a or -R1b in HEK293T cells (p. 674, col. 1 last paragraph; p. 684, last full sentence

of col. 1; and Fig. 3, respectively). Ligand binding was quantified for the expressed GABAB receptors.

Art

The art made of record and not relied upon is considered pertinent to applicant's disclosure. Jones et al. teach a GABABR2 receptor that has a sequence sharing high identity with SEQ ID NO:2 of the instant application, and also teaches heteromeric functional GABAB receptors. Jones et al. is not available as prior art because it was published after the effective filing date of the instant application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

February 21, 2002